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REMARKS

Support for the amendments to Claim 61, parts (vi) and (vii) can be found, *inter alia*, at page 5, third full paragraph of the present specification (the substitute specification filed May 23, 2006), page 6, first full paragraph, and page 26, first and second full paragraphs, in combination with Figures 7A-7B.

On page 5 of the Office Action, the Examiner indicates that Claims 61(i) and 62 are objected to as being dependent upon a rejected base claim, but would be allowable if written in independent form.

Accordingly, Applicants present Claims 61(i) and 62 in independent form in the form of new Claims 67-68. In addition, Applicants present new Claims 69-71, support for which can be found in Claims 64-66.

On page 2 of the Office Action, the Examiner rejects Claims 61 and 63-66 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that the specification lacks written description for the dlgs fragments SEQ ID NOs:4, 6, 8 or 10 binding to Doll.

Further, the Examiner rejects Claim 61 on the basis that the specification does not teach that the fragments, SEQ ID NOs:2, 4, 6 or 10, are able to inhibit tcf-driven luciferase activity in colon cancer cells.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

The substitute specification teaches on page 23, second and third paragraphs, that dLgs and hLgs bind Doll with their

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homology region No. 1 as described in Figure 7A (SEQ ID NOs:2-3) (page 23, second paragraph). Since Lgs is involved in late events of the Wg/Wnt signaling cascade, blocking its function, e.g., by interfering with its interaction with Doll, results in blockage of the Wnt signal propagation. Such blockage may be evidenced by inhibiting tcf-driven luciferase activity in colon cancer cells in a specific reporter assay.

Furthermore, the specification discloses that dLgs and hLgs bind Arm and β -Cat, respectively, with their homology region No. 2, as described in Figure 7B (SEQ ID NOs:4-5) (page 23, second paragraph). Interfering with the interaction of Lgs with β -Cat also results in blockage of the Wnt signal propagation. This also applies where β -Cat is out of control due to oncogenic mutations in such a pathway (page 23, third paragraph).

Thus, even if homology regions No. 1 and No. 2 bind to different components of the Wg/Wnt signaling cascade, i.e., Doll and Arm/ β -Cat, respectively, polypeptides containing either SEQ ID NO:2 or SEQ ID NO:4 are equally suitable to block the Wnt signal propagation, and thus inhibit tcf-drive luciferase activity in colon cancer cells in a specific reporter assay.

Hence, SEQ ID NOs:2 and 4 exhibit the same activity as already shown for the full-length dLgs protein consisting of amino acids 1 to 1464 of SEQ ID NO:23, i.e., both peptides are equally suitable to block Wnt propagation, and thus inhibit tcf-drive luciferase activity in colon cancer cells.

As to SEQ ID NOs:6, 8 and 10, Claim 61 (iii) has been limited to SEQ ID NOs:2 and 4, and Claim 63 has been cancelled.

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In addition, as to Claim 61, it is the Examiner's position that there is no basis for SEQ ID NOs:24 and 25 in the specification where an Xaa is any amino acid.

The sequence homology analysis, onto which SEQ ID NOs:24 and 25 is based, revealed 100% sequence identity for those positions, wherein the amino acids are explicitly identified. These amino acids are expected to be highly correlated with the specific activity of the corresponding peptide, i.e., to block the Wnt signal propagation by binding to β -Cat, and thereby limit tcf-driven luciferase activity in colon cancer cells in a specific reporter assay. In contrast, amino acids in SEQ ID NOs:24 and 25, identified by Xaa, showed a less stringent homology or even no homology in the sequence homology analysis, leading to the conclusion that these amino acids are less or not important for the specific activity of the corresponding peptide. Thus, amino acids in SEQ ID NOs:24 and 25, identified by Xaa, may be substituted by any amino acids.

In any event, "Xaa" and "SEQ ID NOs:24 and 25" have been deleted from the claims and the amendments to Claim 61 (iv) and (v) have been limited to the specific sequences according to SEQ ID NOs:4 and 5, respectively, thereby rendering moot the Examiner's rejection.

Accordingly, Applicants respectfully submit that the claims have written description in the specification, and thus request withdrawal of the Examiner's rejection.

In the paragraph bridging pages 3-4 of the Office Action, the Examiner rejects Claims 61, 63 and 66 under 35 U.S.C. § 102(e) as being anticipated by Venter et al.

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Specifically, the Examiner states that Venter et al's SEQ ID NO:3135 shares 97.2% sequence identity with SEQ ID NO:23, and further the fragments, SEQ ID NOS:2, 4, 6, 8 and 10, are found in the Venter et al sequence. Thus, the Examiner contends that the sequence of Venter et al is a polypeptide "comprising" a fragment of SEQ ID NO:23 where the fragment is SEQ ID NOS:2, 4, 6, 8 or 10.

For the following reasons, Applicants respectfully traverse the Examiner's rejection.

Initially, Applicants note that Claims 62 and 64-65 have not been included in this rejection.

Venter et al does not teach or suggest a polypeptide sequence consisting of the sequence according to SEQ ID NO:23. The Venter et al sequence represents a sequence which lacks the essential alternative start sequence in *Drosophila* and an 40 aa stretch between aa positions 1139 and 1180 in SEQ ID NO:23 (corresponding to nucleic acid positions 5482 to 5601 in SEQ ID NO:1). Due to the missing start sequence, it is unlikely that such a sequence will be expressed in a *Drosophila* cell system. Even if expressed, the lack of the 40 aa stretch can cause a mis-folding of the 3D-structure of the protein, which in turn will most likely lead to loss of its original biological function. Thus, the subject matter of (amended) Claim 61 (i) is not anticipated by Venter et al. The same arguments apply to Claim 61 (ii).

Furthermore, Venter et al does not teach or suggest a fragment of a polypeptide sequence consisting of the sequence according to SEQ ID NO:23, wherein the fragment is a sequence

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according to SEQ ID NOs:2 or 4, and wherein the fragment inhibits tcf-driven luciferase activity in colon cancer cells. In fact, Venter et al discloses a full-length peptide sequence. However, Venter et al fails to disclose that such a sequence may contain essential evolutionary conserved domains. Venter et al also fails to disclose the specific sequence of these domains according to SEQ ID NOs:2 or 4. The domains having the specific sequences according to SEQ ID NOs:2 or 4, and the use of these domains for identifying novel components or interaction partners of Lgs, represent a key aspect of the present invention. Since Venter et al does not disclose the specific sequences, but rather a full-length peptide sequence, and does not even mentions existence of such domains, it is clear that these domains were not yet recognized by Venter et al. Thus, the subject matter of (amended) Claim 61 (iii) is also not anticipated by Venter et al.

Moreover, Venter et al does not disclose or suggest a peptide having at least 90% amino acid sequence identity in the amino acid sequence of SEQ ID NO:4 and 5. These peptides allow a skilled person (based on the disclosure of the present invention) to an assay for, e.g., identify, novel components or interaction partners of Lgs. It is to be emphasized that Venter et al does not allow for such an assay due to its remarkable sequence differences. Thus, Claims 61(iv) and (v) are also not taught by Venter et al.

Accordingly, Applicants respectfully submit that the present invention is not taught or suggested by Venter et al, and thus request withdrawal of the Examiner's rejection.

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On page 4 of the Office Action, the Examiner rejects Claims 61 and 64-66 under 35 U.S.C. § 112, second paragraph.

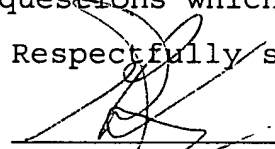
Specifically, the Examiner states that SEQ ID NOs:24 and 25 have 43 and 67% of their amino acids varied, respectively. The Examiner states that it is not clear what the limitation "a polypeptide having at least 90% identity" is because, for example, only 57% of the amino acid sequence of SEQ ID NO:24 is fixed.

"SEQ ID NOs:24 and 25" have been deleted from the claims, thereby rendering moot the Examiner's rejection.

In view of the amendments to the specification and claims, and the arguments set forth above, reexamination, reconsideration and allowance are respectfully requested.

The Examiner is invited to contact the undersigned at his Washington telephone number on any questions which might arise.

Respectfully submitted,



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